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The specific aims of the study are 1) to assess the bone mineral density of women 65 years of age and older with breast cancer in comparison with the bone mineral density of same aged women with normal mammograms; 2) to examine the risk factors associated with breast cancer and low bone mass in these two groups of women; 3) to develop a model based on the study population to determine the predictive value of low bone mass for risk of breast cancer.

During the three years of this study, a total of 300 women (cases with breast cancer and controls with a normal mammogram) aged 65 and older will be recruited from oncology and radiology offices to participate in a study consisting of one clinic visit. At the clinic visit, each subject will complete questionnaires detailing medical history, health habits, reproductive history, and medications. Height and weight will be measured. A blood sample will be drawn for storage. Bone mineral density will be measured at the forearm, hip, lumbar spine (L1-L4), and whole body using dual energy x-ray absorptiometry (DXA).

The results of this study can be used 1) to identify the likelihood of low bone mass in older women with breast cancer; 2) to identify the risk factors that are common to both low BMD and breast cancer; and 3) to determine the feasibility of discontinuing mammography after 65 in women with low bone mass.

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## Table of Contents

## Introduction:

Women with low bone mineral density (BMD) have a low risk for breast cancer. [1,2] Therefore, it has been suggested that mammography may not be worthwhile for older women with low bone density. [3] Measuring BMD at age 65 and stopping mammography in women who have low BMD has been proposed as a cost-effective clinical practice. However, before implementation of this proposal, the question of what proportion of women with breast cancer have low BMD needs to be addressed. The specific aims of the proposed study are 1) to assess the bone mineral density of women 65 years of age and older with breast cancer in comparison with the bone mineral density of same aged women with normal mammograms; 2) to examine the risk factors associated with breast cancer and low bone mass in these two groups of women; 3) to develop a model based on the study population to determine the predictive value of low bone mass for risk of breast cancer. During the three years of this proposed case-control study, a total of 300 women (cases with breast cancer and controls with a normal mammogram) aged 65 and older will be recruited from oncology and radiology offices to participate in a study consisting of one clinic visit. At the clinic visit, each subject will complete questionnaires detailing medical history, health habits, reproductive history, and medications. Height and weight will be measured. A blood sample will be drawn for storage. Bone mineral density will be measured at the forearm, hip, lumbar spine (L1-L4), and whole body using dual energy x-ray absorptiometry (DXA).

## Body:

### Recruitment Phase

At the present time, end of Year 2 of 3, we are still in the recruitment phase for this case-control study. Our study goal was 150 cases of women with newly diagnosed breast cancer and 150 control subjects who have had a normal mammogram. However, we are re-evaluating 1:1 case control ratio and we would achieve greater statistical power using the current number of cases and increasing to 2-3 controls per case. Therefore, we are continuing recruitment of cases and opening up recruitment of additional controls. Cases are defined as women 65 years and older with newly diagnosed breast cancer (within 4 months of their definitive surgical procedure) and control subjects within 4 months of a normal mammogram.

Recruitment has been difficult despite having affirmation of recruitment assistance from multiple sources including hospitals, physicians offices and mailing to age-eligible women identified from voter registration lists. Over the past year we have concentrated on recruitment of cases. Additional resources for recruitment were requested from the sponsor and granted; so that those clinic or hospital staff screening for recruitment of women into the study are compensated for their time. The total number of subjects who have completed the study clinic visit is 106: 57 cases and 49 controls. The ethnicity is 82.1% White (not Hispanic),10.4% Hispanic, 4.7% Asian or Pacific Islander, 2.8% Black or African American.

## Study Clinic Visit

Subjects are seen at the General Clinical Research Center outpatient facility on the UCSD La Jolla campus for one clinic visit. Participants are asked to fast for 12 hours prior to their clinic appointment and to bring in all their medications, including over-the-counter preparations. The clinic visit has been averaging two hours in duration and the following procedures are being performed:

1. Description of the study and administering informed consent before starting any study procedures.
2. Self-administered questionnaires used to obtain information on medical history, family history, health habits detailing smoking history, alcohol consumption, caffeine use, physical activity (Pfaffenberger), and diet (Block Food Frequency).
3. Medications and over-the-counter preparations are validated and recorded detailing the name, dose, frequency, duration, and route of delivery.
4. Height, weight, waist and hip circumferences, and percent body fat from whole body DXA are measured.
5. A fasting sample of blood (30 cc) is drawn for frozen storage and urine sample is collected for frozen storage.
6. Bone mineral density is measured at the forearm, hip, lumbar spine (L1-L4), and whole body using dual energy x-ray absorptiometry (DXA).

## Preliminary Results

For presentation at the annual Era of Hope meeting in September 2002, we analyzed the 57 cases and 49 controls who had completed their study visit. As shown in Table 1, the cases and controls were similar age, years postmenopausal and number of reproductive years. The cases had a higher mean BMI and waist circumference. Their use of current estrogen and other selected lifestyle factors were not significantly different (p>.10).

**Table 1. Characteristics of selected covariates of breast cancer cases and age-matched controls, Breast and Bone Study, San Diego, CA, 2000-2002.**

| Mean values (SD) | Cases (n= 57) | Controls (n=49) | t or $x^2$ | p-value* |
|---|---|---|---|---|
| Age (years) | 72.4  (5.8) | 72.5  (5.3) | -.047 | .963 |
| BMI † | 27.4  (4.7) | 25.5  (5.2) | 1.97 | .051 |
| Waist circumference (cm) | 89.7  (14.0) | 82.8  (12.9) | 2.53 | .013 |
| Hip circumference (cm) | 103.4  (9.7) | 99.9  (10.3) | 1.73 | .087 |
| Years postmenopausal | 25.9  (10.7) | 24.2  (9.8) | .857 | .394 |
| Number of reproductive years ‡ | 33.9  (9.0) | 35.6  (7.1) | -1.02 | .312 |
| Percentages | | | | |
| Current estrogen use** | 55.4 | 65.3 | 1.08 | .324 |
| Current smoking | 7.0 | 4.1 | .43 | .684 |
| Ever smoked | 43.9 | 38.8 | .28 | .693 |

| | | | | |
|---|---|---|---|---|
| Alcohol use (at least 1-2 times/week) | 43.9 | 32.7 | 1.40 | .317 |
| Calcium supplement use | 64.2 | 68.9 | .25 | .672 |
| Breast cancer staging | | | | |
| Stage 0 | 14.6 | | | |
| Stage I | 43.9 | | | |
| Stage II | 41.5 | | | |

\* p value from t-test (continuous variables) or from $x^2$ test (categorical variables)
† Weight (kg)/height (m)$^2$
‡ Number of years between menarche and menopause
\*\* using estrogen at time of breast cancer diagnosis or up to 1 year before diagnosis (cases)

As displayed in Table 2, there were no differences in the bone mineral density at the lumbar spine, hip, forearm, or total body between cases and controls.

**Table 2. Bone mineral densities of breast cancer cases and age-matched controls, Breast and Bone Study, San Diego, CA, 2000-2002.**

| Mean values (SD) | Cases (n= 57) | Controls (n=49) | t | p-value |
|---|---|---|---|---|
| Lumbar spine | .973 (.173) | .962 (.178) | .295 | .768 |
| Femoral neck | .700 (.116) | .678 (.109) | 1.02 | .313 |
| Total hip | .835 (.134) | .791 (.130) | 1.69 | .093 |
| Forearm | .510 (.066) | .505 (.071) | .349 | .728 |
| Total body | 1.014 (.125) | .988 (.099) | 1.18 | .241 |

As shown in Table 3, adjusted odds ratios for breast cancer were did not differ significantly by tertile of bone mineral density at the hip or lumbar spine.

Table 3. Adjusted odds ratios relating breast cancer status with tertiles of bone mineral density, Breast and Bone Study, San Diego, CA, 2000-2002.

| | Breast cancer OR | 95 % CI |
|---|---|---|
| Hip BMD tertile | | |
| 1 † (.453 - .743) | 1.00 | |
| 2 (.744 - .869) | 1.62 | 0.50 – 5.28 |
| 3 (.870 – 1.317) | 1.26 | 0.38 – 4.21 |
| | | |
| Lumbar spine BMD tertile | | |
| 1 † (.561 - .891) | 1.00 | |
| 2 (.892 – 1.016) | 1.35 | 0.42 – 4.38 |

| 3 | (1.017 – 1.572) | 1.93 | 0.58 – 6.43 |
|---|---|---|---|

Adjusted for BMI and current estrogen use
† Referent

In summary, the preliminary results do not shown any differences in bone mineral density at multiple sites between newly diagnosed women with breast cancer in comparison with age-matched women with normal mammograms. Therefore, our preliminary data suggests that bone mineral density would not be useful as prescreening for mammography in older women.

Future plans are continued recruitment of cases and controls. In order to increase the increase the power of this case-control study, we are planning to increase the recruitment of controls with 2-3 controls per case rather than the current 1:1 ratio.

## Key Research Accomplishments:
Not applicable at this time.

## Reportable Outcomes:
Abstract and poster presentation (refer to appendices) were submitted and presented at the 2002 Era of Hope Meeting in Orlando, Florida.

## Conclusions:
Not applicable at this time.

## References:

1.  Cauley J, Lucas F, Kuller L, MT V, Browner WS, Cummings SR. Bone mineral density and risk of breast cancer in older women: The Study of Osteoporotic Fractures. JAMA 1996;276:1404-08.
2.  Zhang Y, Kiel D, Kreger B, et al. Bone mass and the risk of breast cancer among postmenopausal women. New England Journal of Medicine 1997;1997:611-17.
3.  Kerlikowske K, Salzmann P, Phillips K, Cauley J, Cummings SR. Continuing screening mammography in women aged 70 to 79 years. Impact on life expectancy and cost effectiveness. JAMA 1999;282:2156-63.

**Appendices:**

Abstract
Poster

# BREAST CANCER AND BONE MINERAL DENSITY

## Diane L. Schneider, Donna Kritz-Silverstein

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ABSTRACT:

Recent studies have shown that women with low bone mineral density (BMD) have a low risk for breast cancer. Therefore, it has been suggested that mammography may not be worthwhile for older women with low bone density . Measuring BMD at age 65 and stopping mammography in women who have low BMD has been proposed as a cost-effective clinical practice. However, women with newly diagnosed breast cancer have not been evaluated to determine what their BMD levels are at the time of diagnosis. The purpose of our study is to assess the BMD of women 65 years of age and older with newly diagnosed breast cancer in comparison with the bone mineral density of same aged women with normal mammograms and to examine the risk factors associated with breast cancer and low bone mass in these two groups of women.; and to develop a model based on the study population to determine the predictive value of low bone mass for risk of breast cancer.

We are in the process of recruiting women 65 years and older for 150 cases, women with within 4 months of their definitive surgical procedure for breast cancer, and 150 controls, women within 4 months of a normal mammogram. At one clinic visit, subjects complete a health questionnaire. Height, weight, waist and hip girth are measured. Bone mineral density is measured at the hip, spine, forearm, and total body by dual energy x-ray absorptiometry (Hologic QDR 2000).

Preliminary results from 24 cases and 42 controls were evaluated. The mean age for both groups is 72 years. Bone mass index is higher in cases than controls, 27.1 ( ±4.1 SD) versus 26.2 (±6.0 SD). Bone mineral density at the total hip was lower in the cases in comparison with the controls, 0.785 g/cm2 (±0.108 SD) and 0.795 (±0.127 SD), respectively. At the lumbar spine, the mean BMD was also lower in the cases, 0.933 (±0.126 SD), than controls, 0.978 (±0.182 SD).

In the first group of women evaluated for this study, the BMD of women with newly diagnosed breast cancer is lower than controls. However, the results of this study are preliminary and cannot be yet be used to make any conclusions.

# BREAST CANCER AND BONE MINERAL DENSITY

Diane L Schneider, Donna Kritz-Silverstein, Julie Sandwell.
University of California San Diego

## ABSTRACT

Recent studies have shown that women with low bone mineral density (BMD) have a low risk for breast cancer. Therefore, it has been suggested that mammography may not be worthwhile for older women with low bone density. Measuring BMD at age 65 and stopping mammography in women who have low BMD has been proposed as a cost-effective clinical practice. However, women with newly diagnosed breast cancer have not been evaluated to determine what their BMD levels are at the time of diagnosis. The purpose of our study is to assess the BMD of women 65 years of age and older with newly diagnosed breast cancer in comparison with the bone mineral density of same aged women with normal mammograms and to examine the risk factors associated with breast cancer and low bone mass in these two groups of women; and to develop a model based on the study population to determine the predictive value of low bone mass for risk of breast cancer.

We are in the process of recruiting women 65 years and older for 150 cases, women with within 4 months of their definitive surgical procedure for breast cancer, and 150 controls, women within 4 months of a normal mammogram. At one clinic visit, subjects complete a health questionnaire. Height, weight, waist and hip girth are measured. Bone mineral density is measured at the hip, spine, forearm, and total body by dual energy x-ray absorptiometry (Hologic QDR 2000).

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***The U.S. Army Medical Research Materiel Command under DAMD17-00-1-0185 supported this work.***

## BACKGROUND

- ◆ **Recent studies have shown that women with low bone mineral density (BMD) have a low risk for breast cancer.**
- ◆ **It has been suggested that mammography may not be worthwhile for older women with low bone density .**
- ◆ **Measuring BMD at age 65 and stopping mammography in women who have low BMD has been proposed as a cost-effective clinical practice.**
- ◆ **Women with newly diagnosed breast cancer have not been evaluated to determine what their BMD levels are at the time of diagnosis.**

### AIM

**The purpose of our study is to assess the BMD of women 65 years of age and older with newly diagnosed breast cancer in comparison with the bone mineral density of same aged women with normal mammograms and to examine the risk factors associated with breast cancer and low bone mass in these two groups of women.**

## METHODS

**STUDY POPULATION**

- ■ 106 postmenopausal women
- ■ Aged 65 to 88 years; mean age 72.5 years
- ■ 57 cases with newly diagnosed breast cancer
  - -within 4 months of definitive surgery
  - -prior to chemotherapy
  - -no use of bisphosphonates or calcitonin
- ■ 49 matched controls (match on age)
  - -within 4 months of normal mammogram
  - -no use of bisphosphonates or calcitonin

**DATA COLLECTION (2000-2002)**

- ■ Standardized questionnaire (medical history, health habits, dietary supplements, and medications)
- ■ Measured height and weight
- ■ BMD (g/cm²) at hip, lumbar spine, forearm, and total body by DXA
  - ◆ (Hologic QDR 2000)
- ■ Medical record verification of cases for diagnosis & staging

**STATISTICAL ANALYSES**

- ■ Comparisons used t-tests for continuous variables and chi-square for categorical variables
- ■ Odds ratios for risk of breast cancer were calculated with logistic regression adjusting for BMI, and current estrogen use

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| Years postmenopausal | 25.9 (10.7) | 24.2 (9.8) | .657 | .394 |
| Number of reproductive years ‡ | 33.9 (9.0) | 35.6 (7.1) | -1.02 | .312 |
| Percentages | | | | |
| Current estrogen use | 12.3 | 65.3 | 31.86 | .000 |
| Current smoking | 7.0 | 4.1 | .43 | .684 |
| Ever smoked | 43.9 | 38.8 | .28 | .693 |
| Alcohol use (at least 1-2 times/week) | 43.9 | 32.7 | 1.40 | .317 |
| Calcium supplement use | 64.2 | 68.9 | .25 | .672 |
| Breast cancer staging | | | | |
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* p value from t-test (continuous variables) or from $x^2$ test (categorical variables)
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| 3 (1.017 – 1.572) | 1.93 | 0.58 – 6.43 |

Adjusted for BMI and current estrogen use
† Referent

## RESULTS

**TABLE 1**

- ◆ **Women were age-matched.**
- ◆ **Cases had higher BMIs, waist and hip circumferences.**
- ◆ **Current estrogen defined as use within the past 4 months was significantly lower in the cases.**

**TABLE 2**

- ◆ **Bone mineral density was similar at all measured sites**

**TABLE 3**

- ◆ **Adjusted odds ratios were not significantly different between tertiles of bone mineral density at the hip or lumbar spine**

## LIMITATIONS

- ■ **These are preliminary results.**
- ■ **Limited number of subjects thus far, therefore results may not reflect truth.**
- ■ **Unable to determine which participants stopped hormone use based on abnormal mammogram.**

## CONCLUSION

☆ **In this small case-control study, there were no differences in bone mineral density between the women with new diagnosed breast cancer and controls.**

☆ **Therefore, bone mineral density would not be useful as prescreening for mammography in older women.**